Appendix S5-1. Description of Risk of Bias in Case-Control Studies, Cross-Sectional Studies and Case Series

First	1. Sample o	f Patients		2. Outco	ome		3. Expos	sure		4. Analysis	
Author,	Eligibility	Sample	Represent	Fully	Blinded to	Known	Fully	Blinded to	Known	Confounding Factors	Appropria
Year,	Criteria	Selection	ativeness	Define	Exposure	for All	Define	Outcome	for All	Adjusted for	te
(Reference			in	d	Status	Subjects	d	Status	Subjects		Analysis
No.)			Controls			?			?		
Beasley,	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R	none	good
1982 [22]											
Chang,	good	poor <sup>b</sup>	poor <sup>d</sup>	poor <sup>e</sup>	N/A	100%	good	N/R	65%	matched on age	poor <sup>e</sup>
1989 [23]											
Hsu, 1988	poor <sup>a</sup>	poor <sup>c</sup>	N/A	good	N/R	100%	poor <sup>g</sup>	N/R	67%	none	good
[24]											
Wheeley,	poor <sup>a</sup>	poor <sup>c</sup>	N/A	good	N/R	100%	good	N/A	90%	none	poor <sup>m</sup>
1989 [29]											
Habu, 1991	poor <sup>a</sup>	poor <sup>c</sup>	N/A	good	N/R	100%	poor <sup>h</sup>	N/R	100% <sup>k</sup>	stratified by age group	good

good	good	N/A	good	N/R	90%	poor <sup>i</sup>	N/R	52%	none	poor <sup>m</sup>	
N/R	poor <sup>c</sup>	N/A	poor <sup>h</sup>	N/R	89%	poor <sup>g</sup>	N/R	49%	adjusted for age	good	
good	poor <sup>c</sup>	N/A	good	N/R	100%	poor <sup>g</sup>	N/R	75%	none	good	
good	good	good	good	good	100%	good	N/R	100%	adjusted for age, sex,	poor <sup>n</sup>	
									smoking, anti-HCV,		
									HBsAg and sibship size		
good	poor <sup>b</sup>	good	poor <sup>e</sup>	N/A	100%	good	N/R	99% for	matched on age and sex,	poor <sup>l, n</sup>	
								cases and	adjusted for age, sex,		
								97% for	schooling, smoking,		
								controls			
									and sibship size		
	N/R good	N/R poor <sup>c</sup> good poor <sup>c</sup> good good	N/R poor <sup>c</sup> N/A  good poor <sup>c</sup> N/A  good good good	N/R poor <sup>c</sup> N/A poor <sup>h</sup> good poor <sup>c</sup> N/A good  good good good good	N/R poor <sup>c</sup> N/A poor <sup>h</sup> N/R  good poor <sup>c</sup> N/A good N/R  good good good good	N/R poor <sup>c</sup> N/A poor <sup>h</sup> N/R 89%  good poor <sup>c</sup> N/A good N/R 100%  good good good good 100%	N/R poor N/A poor N/R 89% poor poor good poor N/A good N/R 100% poor good good good 100% good	N/R poor <sup>c</sup> N/A poor <sup>h</sup> N/R 89% poor <sup>g</sup> N/R  good poor <sup>c</sup> N/A good N/R 100% poor <sup>g</sup> N/R  good good good good good 100% good N/R	N/R poor N/A poor N/R 89% poor N/R 49%  good poor N/A good N/R 100% poor N/R 75%  good good good good good 100% good N/R 100%  good N/R 99% for cases and 97% for	N/R poor N/A poor N/R 89% poor N/R 49% adjusted for age good poor N/A good N/R 100% poor N/R 75% none good good good good good good 100% good N/R 100% adjusted for age, sex, smoking, anti-HCV, HBsAg and sibship size good poor good poor N/A 100% good N/R 99% for matched on age and sex, cases and adjusted for age, sex, good N/R 99% for schooling, smoking, controls alcohol, anti-HCV, HBsAg	

Tai, 2002	good	good	N/A	good	N/R	95%	good	N/R	100%	stratified by relationship	good
[34]										with index case	
Cai, 2003	good	poor <sup>c</sup>	N/A	good	N/R	100%	poor <sup>j</sup>	N/A	100%	none	poor <sup>o</sup>
[36]											
Cao, 2005	good	poor <sup>c</sup>	N/A	$poor^{f}$	N/R	100%	poor <sup>j</sup>	N/A	100%	none	poor <sup>o</sup>
[37]											
Song, 2009	good	good	N/A	good	N/R	96%	poor <sup>j</sup>	N/A	100%	none	poor <sup>o</sup>
[38]											

Abbreviations: HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus; N/A, not applicable; N/R, not reported.

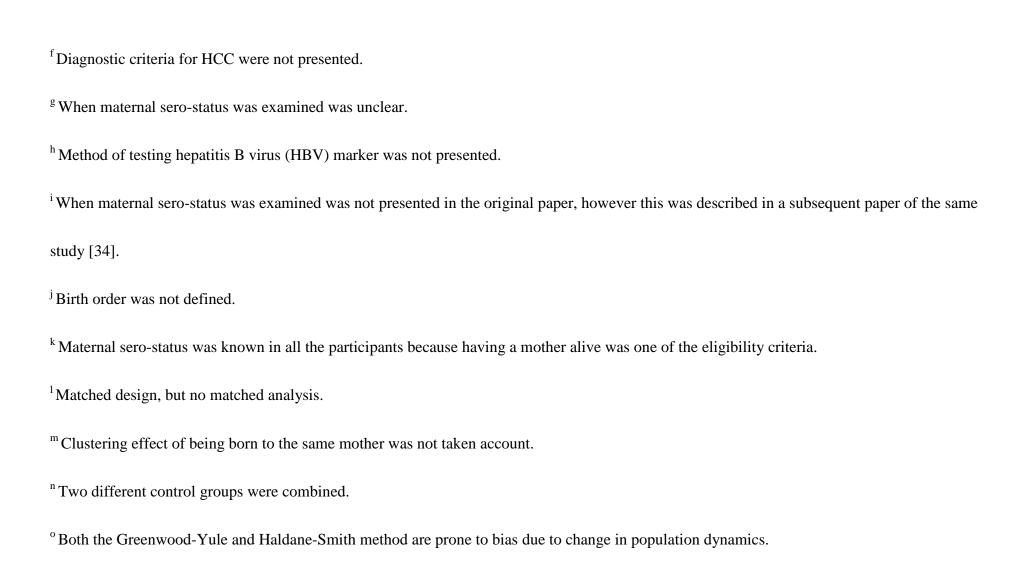
<sup>&</sup>lt;sup>a</sup> Definition of HBsAg carrier was not presented.

<sup>&</sup>lt;sup>b</sup> The way of selecting control subjects was unclear.

<sup>&</sup>lt;sup>c</sup> Setting of sample selection was unclear.

<sup>&</sup>lt;sup>d</sup> Hospital-based cases were compared with population-based controls.

<sup>&</sup>lt;sup>e</sup> Cut-off value of alpha fetoprotein (AFP) for hepatocellular carcinoma (HCC) diagnosis was not presented.



Appendix S5-2. Description of Risk of Bias in Cohort Studies

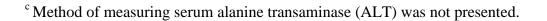
First	1. Sample	of Patients		2. Follow up	3. Outcome			4. Exposure			5. Analysis		6.
Author,													Treatment
Year,													After
(Referenc													Inclusion in
e No.)													Cohort
	Eligibilit	Sample	Assemble	Sufficiently	Fully	Blinde	Known	Fully	Blinded	Known	Confoun	Appropr	Fully
	y	Selection	d at a	Long	Define	d to	for all	Defined	to	for all	ding	iate	Described
	Criteria		Common		d	Exposu	Subjec		Outcom	Patient	Factors	Analysis	
			Stage			re	ts?		e Status	s?	Adjuste		
						Status					d for		
McMahon,	good	poor <sup>b</sup>	Good	good	good	N/R	100%	poor <sup>e</sup>	N/A	100%	N/R	poor <sup>i</sup>	poor <sup>j</sup>
2001 [21]													
Kojima,	poor <sup>a</sup>	poor <sup>b</sup>	Good	good	poor <sup>c</sup>	N/R	100%	poor <sup>f</sup>	N/R	100% <sup>h</sup>	N/R	poor <sup>i</sup>	good (no
1985 [25]													treatment)

Tseng, good poor <sup>b</sup> Good good good N/R 100% good N/R 95% adjusted good good (no														
Chang, good poor Good good good N/R 100% poor N/R 95% Stratified poor good (no. 1989 [27]	Kojima,	poor <sup>a</sup>	poor <sup>b</sup>	Good	good	poor <sup>d</sup>	N/R	100%	poor <sup>f</sup>	N/R	72%	N/R	poor <sup>i</sup>	good
1989 [27] Tseng, good poor Good good good N/R 100% good N/R 95% adjusted good good no genotype 2011 [28]  HBV  HBV	1985 [26]													(steroid)
Tseng, good poor Good good good N/R 100% good N/R 95% adjusted good good (no genotype and genoty	Chang,	good	poor <sup>b</sup>	Good	good	good	N/R	100%	poor <sup>g</sup>	N/R	95%	Stratified	poor <sup>i</sup>	good (no
Tseng, good poor <sup>b</sup> Good good good N/R 100% good N/R 95% adjusted good good (no good (no good))  2011 [28]  Good good N/R 100% good N/R 95% adjusted good good (no good)  genotype  and  maternal  HBV	1989 [27]											by age		treatment)
2011 [28] for HBV treatment) genotype and maternal HBV												group		
genotype and maternal HBV	Tseng,	good	poor <sup>b</sup>	Good	good	good	N/R	100%	good	N/R	95%	adjusted	good	good (no
and maternal HBV	2011 [28]											for HBV		treatment)
maternal HBV												genotype		
HBV												and		
												maternal		
marker												HBV		
												marker		

Abbreviations: HBV, hepatitis B virus; N/A, not applicable; N/R, not reported.

<sup>&</sup>lt;sup>a</sup> Definition of hepatitis B surface antigen (HBsAg) carrier was not presented.

<sup>&</sup>lt;sup>b</sup> Setting of sample selection was unclear.



<sup>&</sup>lt;sup>d</sup> Method of testing HBV marker was not presented.

<sup>&</sup>lt;sup>e</sup> How often blood sample was obtained to determine timing of HBV infection was not reported.

<sup>&</sup>lt;sup>f</sup> When maternal sero-status was examined was not presented in this paper, but this was confirmed by the communication with the author.

<sup>&</sup>lt;sup>g</sup> When maternal sero-status was examined was unclear.

<sup>&</sup>lt;sup>h</sup> Maternal sero-status was known in all the participants because having a mother tested was one of the eligibility criteria.

<sup>&</sup>lt;sup>i</sup> Person-years at risk were not taken account in the analysis.

<sup>&</sup>lt;sup>j</sup> For the sub-study of patients with known age at HBV infection, number of those who were treated was not reported.